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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/721,563	11/25/2003	Tal Kafri	9435-2	5850

7590 07/18/2005

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EXAMINER	
BURKHART, MICHAEL D	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 07/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/721,563	KAFRI ET AL.	
	Examiner	Art Unit	
	Michael D. Burkhart	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *23-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,12-17,19 and 21-23* is/are rejected.

7)☒ Claim(s) *11,18 and 20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11/25/2003 and 5/12/2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/8/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of Group I, claims 1-23, in the reply filed on 4/19/2005 is acknowledged. The traversal is on the ground(s) that to search both Groups I and II would not be burdensome because the searches would overlap, and applicants also contend that the proper requirements for restriction (primarily burdensome search) have not been met. This is not found persuasive because, as stated in the Restriction Requirement, the different inventions have separate classifications. As explained by applicants on page 2 of the Response dated 4/19/2005, a separate classification is *prima facie* evidence of a burdensome search. Furthermore, as stated on page 3 of the Restriction Requirement, a separate search was deemed to be required for the two Groups. This is due to the need to search and evaluate the art for the distinct compositions and method steps found in Group II relative to Group I, primarily cDNA libraries, evaluating test substances and phenotype, and Cre protein.

The requirement is still deemed proper and is therefore made FINAL.

Claims 24-29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 4/19/2005.

Claim Objections

Claim 20 is objected to because of the following informalities: "HIV-form" should be "HIV-1 form" in order to agree with the proceeding claim language. Appropriate correction is required.

Claims 11 and 18 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 23 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 23 recites the limitation "A retroviral expression vector" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, 5, 8, 9, 12, 13, 16, 19, 21, and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Miyoshi et al (J. Virol., 1998, reference 8 of the 9/8/2004 IDS). The claims recite an isolated nucleic acid and vector comprising a single retroviral long terminal repeat (LTR), a polypurine tract, a packaging signal, a primer binding site, and a rev responsive element

(RRE). The nucleic acid and vector may also comprise a eukaryotic promoter, a bacterial origin of replication, and a bacterial selection marker. The LTR may have a major portion of the U3 region deleted and the U3 may comprise a restriction site. Also claimed are a nucleic acid and vector comprising the elements above and an additional LTR, so that the 5' and 3' LTRs are present. The bacterial elements are located between the LTRs. Also claimed is a method of making a retroviral particle by introducing the above vector into a packaging cell comprising nucleic acid sequences encoding rev, gag/pol, and env proteins but lacking packaging sequences, followed by collecting the particles from the cell medium. Claim 22 recites a method to produce a retroviral expression vector by cloning the above nucleic acid into a non-retroviral expression vector.

For purposes of examination, and because the specification does not specifically describe what does and does not constitute an LTR, it is considered that if significant portions (such as the U3) of an LTR are replaced such that it no longer has the characteristics of a wild-type LTR, than it can no longer be considered an LTR. Miyoshi et al teach such vectors, CL-CG for example, in which the 5' LTR has a CMV promoter in place of the U3, and thus no longer is Tat-dependent for transcription, an LTR function (see abstract and Fig. 1, page 8152). Thus, CL-CG has one LTR. CL-CG was prepared from pHR', which comprises an RRE, a packaging signal (Ψ), a primer binding site (PBS), and a polypurine tract (PPT). See the description of pHR' in Naldini et al (Science, 1996, Fig. 1) and Naldini et al (PNAS, 1996, Fig. 1). The retroviral PBS is located immediately after the U5 region of the 5' LTR, and the PPT immediately adjacent to the 3' LTR (See Rausch et al, Int. J. Biochem. Cell Biol., 2004, Fig. 1) and both are required for reverse transcription. The pHR' plasmid was prepared from pR9 (see attached map and

references within the Naldini papers) which has a bacterial origin of replication and encodes ampicillin resistance. CL-CG also contains a eukaryotic promoter (CMV). Also disclosed are vectors with deletions in the U3 of the 3' LTR (Fig. 1, CS-CG vector, and abstract) which are considered major according to applicants description on page 9 of the specification. The U3 region of the LTR contains numerous restriction sites, see the first paragraph of column 1, page 8151. Also disclosed are vectors with both the 5' and 3' LTRs and heterologous genes, for example, LL-CG and LS-CG, which have the same characteristics as listed above for the CL-CG and CS-CG and the bacterial elements are located between the LTRs, (see for example the attached pR9 map). The vectors are used to prepare retroviral particles by transfecting 293T cells with the vectors along with vectors encoding gag/pol, rev (pCMVΔR8.2), and env (pMD.G), see second paragraph, first column, page 8151. Also see the Naldini et al references above for descriptions of the pCMVΔR8.2 and pMD.G plasmids, which do not have packaging signals. According to the specification (page 12), the non-retroviral expression vector can be " ..any expression vector into which the KM fragment can be cloned according to standard methods of cloning". Thus, the pR9, and the pHR' vectors derived from pR9, into which Miyoshi et al cloned the nucleic acids described above, are considered to be non-retroviral expression vectors.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2, 3, 6, 7, 10, 14, 15, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miyoshi et al (cited above) in view of Xu et al (Jan., 2001, reference 15 of the 9/8/2004 IDS).

The claimed nucleic acids and vectors are described above, and may also comprise a central polypurine tract, a post-transcriptional regulatory element, and the deleted portion of U3 may be replaced with an inducible promoter.

The teachings of Miyoshi et al are described above and applied as before.

Miyoshi et al does not explicitly teach the use of a central polypurine tract, a post-transcriptional regulatory element, and that the deleted portion of U3 may be replaced with an inducible promoter.

Xu et al teach the addition of a central polypurine tract and the woodchuck hepatitis virus posttranscriptional regulatory element to lentivirus vectors prepared from the CL and CS-CG vectors of Miyoshi et al, and that the reason for this was to improve nuclear import of the vector

and to increase transgene expression (see Fig. 3 and page 100, second column). Xu et al further teaches the introduction of an inducible promoter (TRE) into the U3 region of the 3' LTR, and that the reason for this was to allow transcription and packaging of the virus in packaging cells only, inactivating the virus upon infection of target cells. See page 97, Introduction, Fig. 1 and Fig. 3.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teachings of Miyoshi et al to include the use of a central polypurine tract, a woodchuck hepatitis virus posttranscriptional regulatory element, and an inducible promoter because it was known in the art at the time of filing that these elements can improve the efficiency of the vector and transgene expression, and because Xu et al teach these modifications are desirable for reasons of biosafety and for producing stable producer (or packaging) cell lines. One would have been motivated to do so in order to receive the expected benefit of improving the vectors and methods taught by Miyoshi et al by increasing efficiency of particle production and infection, transgene expression, and improvement of biosafety. Given the teachings of the cited art, the state of the art at the time of applicants invention, and absent evidence to the contrary, there would have been a reasonable expectation of success in introducing the central polypurine tract, woodchuck hepatitis virus posttranscriptional regulatory element, and an inducible promoter taught by Xu et al into the nucleic acids and vectors taught by Miyoshi et al.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael D. Burkhart whose telephone number is (571) 272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael D. Burkhart
Examiner
Art Unit 1633

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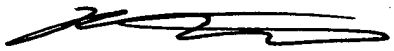
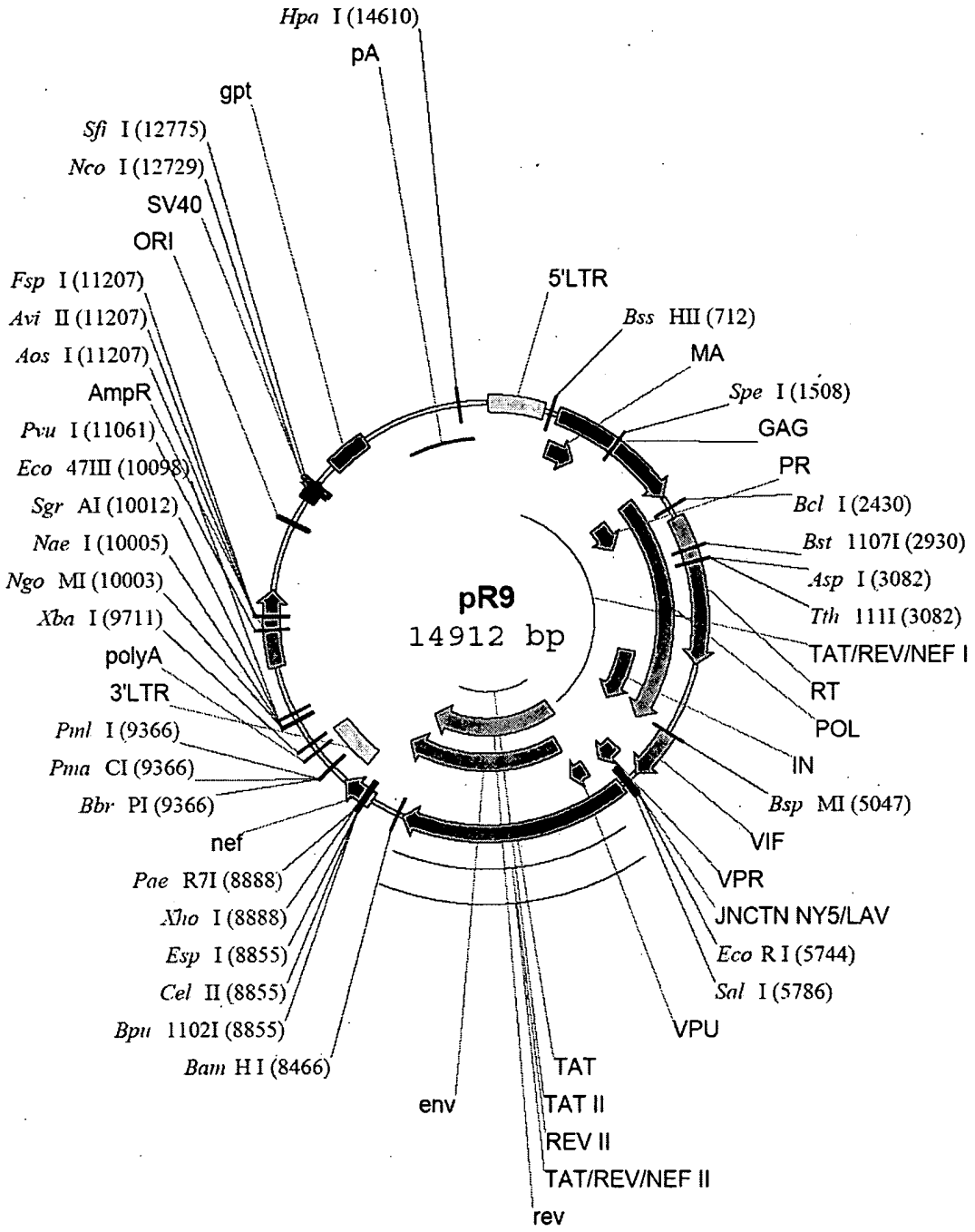
PATENT EXAMINER

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